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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,509	04/19/2006	Philippe Chatellard	ARS-127	6271

23557 7590 06/20/2008

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
06/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,509	CHATELLARD ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-51* is/are rejected.

7)☒ Claim(s) *31-51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 April 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/6/08;7/2/07;4/19/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Claims 31-51 are presently pending, from the preliminary amendment of 4/19/06.

Claims 31-51 are presently considered.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because Figure 1 is objected to because it is a sequence alignment, as further denoted by the specification, in the brief description of the drawings; however, the alignment is not aligned. It is recommended to submit a new figure 1, with the proper alignment provided. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Specifically the application fails to comply with CFR 1.821(d), which states:

(d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier,

preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

The specification discloses nucleotide sequences in Figure 1. However, these sequences are not identified by sequence identifiers in the brief description of the figures.

For compliance with sequence rules, it is necessary to include the sequence in the "Sequence Listing" and identify them with SEQ ID NO. In general, any sequence that is disclosed and/or claimed as a sequence, i.e., as a string of particular bases or amino acids, and that otherwise meets the criteria of 37 CFR 1.821(a), must be set forth in the "Sequence Listing." (see MPEP 2422.03).

For the response to this office action to be complete, Applicants are required to comply with the Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

List of References in Specification

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claims 31-51 are objected to because of the following informalities:

Claim 31 recites a Markush-type group of elements for compositions. Elements 31(l) and 31(m) comprise the same compositions, listed in different orders, but such orders does not

provide for distinct structures, and hence, these elements are the same element, which requires deletion of one element.

Similarly, elements 31(n)(L) and 31(n)(M) comprise the same compositions, listed in different orders, but such orders does not provide for distinct structures, and hence, these elements are the same element, which requires deletion of one element.

Claims 32-51 are objected to for depending from an objected-to base claim.

Appropriate correction is required.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant is advised that should claim 40 be found allowable, claim41 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 40 and 41 differ in only their order of listing which subunit is the alpha or beta chain, but such order of listing does not provide a structural distinction for the composition, and hence, despite a slight difference in wording, the claims are substantial duplicates.

Applicant is advised that should claim 42 be found allowable, claim 43 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 42 and 43 differ in only their order of listing which subunit is the alpha or beta chain, but such order of listing does not provide a structural distinction for the composition, and hence, despite a slight difference in wording, the claims are substantial duplicates.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 46-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 46 recites a method for producing a protein, however, the sole method step is transforming a cell. Hence, due to the lack of a conclusion of commensurate with the preamble, and sole method step which does not make it patently clear to the Artisan that the method is

complete, the Artisan could not determine whether or not the claim is complete. Hence, the metes and bounds of the claim are not clear.

Claims 47-51 are rejected for depending from a rejected base claim, and not overcoming the lack of clarity in such base claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 46-51 encompass making a polypeptide of interest, such method comprising transfecting a host cell with a vector comprising the polypeptide of interest. Dependent Claim 47 requires the method to also comprise culturing the cell. Dependent claims 48-51 depend from either Claim 46 or 47, and further require isolation of the polypeptide of interest, or the transfection of the host cell to be stable.

The first, and most important, aspect, is that the vector is not required to code for the polypeptide of interest. However, as is taught throughout the specification, and is known in the Art, the vector must encode the polypeptide, so that the cell may make the polypeptide via standard expression mechanisms. Nothing is known in the Art of a cell which can replicate a

protein, just by being transformed with a vector comprising the protein. Hence, for this aspect, the Artisan would have to perform undue experimentation to find those cell types which would replicate proteins from vectors which have transformed the cell.

Further, comparing Claims 47 and 46, such distinct difference indicates that Applicant is specifically claiming, in Claim 46, the absence of a culturing step. However, it is well known in the Art, and as shown in the specification and examples by Applicant, that cells require time to transcribe and translate sequences from vectors in order to produce protein, such protein production is not instantaneous. Hence, it would be undue experimentation to find those vectors and cell combinations which allow for instantaneous protein production after transformation.

Such experimentation is undue as it amounts to inventing the breadth of Applicant's claimed invention for Applicant. Hence, the claims lack an enabling disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-33, 36-38 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,395,549 to Tuan, et al., Recillas-Targa, et al. (2002) Proceedings of the National Academy of Sciences, USA, 99(10) 6883-88), Chung, et al. (1997) Proceedings of the National Academy of Sciences, USA, 94: 575-80, and U.S. Patent No. 6,432,700 to Henderson, et al.

Tuan teaches integrating vectors comprising enhancers, insulators, and promoters to drive the expression of any gene of interest in animal cells (ABSTRACT). Further, it is taught to use barrier-function sequences to isolate the integrated vector from position effects in the chromatin to avoid silencing (e.g., Detailed Description of the Invention, paragraph 5). Hence, Tuan teaches that it is known in the Art to place barrier-function sequences on both sides of an integrating vector in order to protect it from silencing, and this can be used for the expression of desired transgenes. Further Tuan teaches the use of GFP coding sequences as a reporter for expression (e.g., paragraph preceding "Constructs and Vectors), and further to link the expression of such GFP to hCMV to obtain expression in cells (e.g., Figure 8), as it is well known that such promoters are widely active in many cell types. Hence, the Artisan would know that the use of a GFP coding sequence would allow quick identification of transformed cells, as is standard in the Art to identify the transformed and expressing cells.

Recillas-Targa teaches that the position protection effect of the chicken beta-globin insulator is located in a larger region encompassed by Applicant's SEQ ID NO: 1 (e.g., Figure 1), and is severable from the enhancer blocking activity (e.g., TITLE). Further, Recillas-Targa teaches that it is normal to utilize two copies of the position-effect on both sides of the vector provide for good isolation from position effects (e.g., p. 6885, col. 2, paragraph 3). Lastly, Recillas-Targa teaches minimization of domain sizes (e.g., whole article).

Chung teaches that the same insulator as Recillas-Targa is active in mammalian cells (e.g., p. 576, col. 2, paragraph 2).

Henderson teaches that it is optimal to minimize the size of the other components of the vector, in order to make more room for transgenes which are to be expressed (e.g., col. 17, paragraph 1).

Hence, from this, the Artisan would be motivated to make an integrating vector, comprising two copies of SEQ ID NO 1 on each end of the integrating vector, with the normally-present base that Applicant has removed from the sequence, and further to comprise the the CMV promoter driving expression of GFP. The Artisan would be so-motivated to provide the minimal sequence of the beta-globin barrier sequence of Recillas-Targa, and do so to express proteins in mammalian cells, as is taught in Chung. In addition, there is a reasonable expectation of success, as the use of such barriers was known, the methods of minimization were known, and the methods of utilizing such to express proteins from integrated vectors was known.

However, such, in itself, does not make obvious the further deletion of the base which Applicant's SEQ ID NO: 1 is missing, from that of the known sequence of the chicken beta globin insulator/barrier sequence.

On the other hand, it is clear that the Artisan knew that the important sequences for the barrier functions were those regions that did not bind proteins (e.g., Recillas-Targa, DISCUSSION), and that intervening sequences were not known to be important. Moreover, Applicant's deleted base is within the intervening sequences (e.g., Chung, FIGURE 3, line 5 of the sequence, the penultimate "C" in such line, determined by comparison to Applicant's specification, FIGURE 1).

Hence, it would be obvious to further delete the "C" between the binding regions. The Artisan would have done so to further minimize the size the barrier region. Further the Artisan

would have expected success, as such region was not bound by any proteins which cause the barrier effect.

Therefore, the Artisan would make these integrating vectors and transform mammalian cells with such vectors to express transgenes, including GFP for identification of those cells expressing the transgene. The Artisan would have expected success, as the methods were known in the Art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-34, 36-41, 44, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,395,549 to Tuan, et al., Recillas-Targa, et al. (2002) Proceedings of the National Academy of Sciences, USA, 99(10) 6883-88), Chung, et al. (1997) Proceedings of the National Academy of Sciences, USA, 94: 575-80, and U.S. Patent No. 6,432,700 to Henderson, et al. as applied to claims 31-33, 36-38 and 44 above, and further in view of Perlman, et al. (2003) The Journal of Clinical Endocrinology & Metabolism, 88(7): 3227-35.

As shown above, the Art teaches various claims, but does not teach the polypeptide of interest being FSH alpha and beta subunits, or the use of CHO cells.

On the other hand, Perlman teaches that CHO cells can be used to express FSH from vectors comprising the alpha and beta subunits (e.g., p. 3228, col. 1).

Hence, it would be further obvious to transform CHO cells with such vectors carrying the alpha and beta subunits of FSH. The Artisan would be motivated to do so in order to express FSH from the cells. Moreover, the Artisan would have a reasonable expectation of success, as the cells were already known for expression of FSH.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-33, 35-38 and 44 rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,395,549 to Tuan, et al., Recillas-Targa, et al. (2002) Proceedings of the National Academy of Sciences, USA, 99(10) 6883-88), Chung, et al. (1997) Proceedings of the National Academy of Sciences, USA, 94: 575-80, and U.S. Patent No. 6,432,700 to Henderson, et al. as applied to claims 31-33, 36-38 and 44 above, and further in view of U.S. Patent No. 6,194,152 to Laus, et al.

As shown above, the Art teaches various claims, but does not teach the transgene for expressing thymidine kinase.

On the other hand, Laus teaches expression of thymidine kinase transgenes as a selectable marker in mammalian cells (e.g., section titled "c. Expression in Mammalian Systems", paragraph 7).

Hence, it would be further obvious to modify the vectors to comprise the thymidine kinase transgene as a marker for mammalian cell expression. Moreover, the Artisan would have a reasonable expectation of success, as such markers were well known in the Art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-33, 36-39 and 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,395,549 to Tuan, et al., Recillas-Targa, et al. (2002) Proceedings of the National Academy of Sciences, USA, 99(10) 6883-88), Chung, et al. (1997) Proceedings of the National Academy of Sciences, USA, 94: 575-80, and U.S. Patent No. 6,432,700 to Henderson, et al. as applied to claims 31-33, 36-38 and 44 above, and further in view of U.S. Patent No. 6,113,898 to Anderson, et al.

As shown above, the Art teaches various claims, but does not teach the use of CHO cells, or the expression of the heavy and light chains of an immunoglobulin.

On the other hand, Anderson teaches CHO cells being transformed to express the heavy and light chains of antibodies to to the human B7.1 and/or B7.2 antigens (e.g., Summary of the Invention, penultimate paragraph).

Hence, at the time of invention, it would have been obvious to further modify the vector to comprise the coding sequences of the heavy and light chains of such antibodies. The Artisan would do so in order to express such in CHO cells. Moreover, there is a reasonable expectation of success, as Anderson teaches such expression.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Examiner of Art Unit 1633